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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,165	08/27/2001	David B. MacLean	PC10616ATMC	4378

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EXAMINER
HUI, SAN MING R

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/940,165	MACLEAN, DAVID B.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 17-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 17-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendments filed August 31, 2004 have been entered.

Applicant's election of the specie 2-amino-N-[2-(3a-(R)-benzyl-2-methyl-3-oxo-2,3,3a,4,6,7-hexahydro-pyrazolo[4,3c]pyridine-5-yl)-1-(R)-benzyloxymethyl-2-oxo-ethyl]isobutyramide in the reply filed on March 25, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The cancellation of claims 15-16 and 27-30 in applicant's amendments filed August 31, 2004 is acknowledged.

Claims 1-14 and 17-26 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12, 17-18, and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for specific disclosed growth hormone secretagogue (GHS) listed in page 10 of the instant specification, does not reasonably provide enablement for other GHSs. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. In the instant case, the

specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that define a "growth hormone secretagogue ". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of "growth hormone secretagogue" examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the class of compounds required. The structural differences among the compounds are great. The only common properties among these compounds are their function as growth hormone secretagogue. The

pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on **all** "growth hormone secretagogue", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

Response to arguments

Applicant's arguments filed August 31, 2004 averring the definition of growth hormone secretagogue (GHS) being set forth in the instant specification have been considered, but are not found persuasive. It is not the definition, but the criteria that the instant specification set forth in selecting a suitable GHS compounds is in question. There is no specific structural, physical, or chemical characteristics of the compounds recited disclosed in the instant specification. By functionally defining what the compounds intended to be encompassed by the claims, applicant is essentially defining the instant method by using functional language at point of novelty. Attention is directed to *General Electric Company v. Wabash Appliance Corporation et al* 37 USPQ 466 (US 1938), at 469, speaking to functional language at the point of novelty as herein employed: "the vice of a functional claim exists not only when a claims is "wholly" functional, if that is ever true, but when the inventor is painstaking when he recites what has already been seen, and then uses conveniently functional language at the exact point of novelty". Functional language at the point of novelty, as herein employed by Applicants, is further admonished in *University of California v. Eli Lilly and Co.* 43

USPQ2d 1398 (CAFC 1997) at 1406: stating this usage does "little more than outlin[e] goals appellants hope the recited invention achieves and the problems the invention will hopefully ameliorate". Applicants functional language at the point of novelty fails to meet the requirements set forth under 35 USC 112, first paragraph. Claims employing functional language at the point of novelty, such as Applicants', neither provide those elements required to practice the inventions, nor "inform the public during the life of the patent of the limits of the monopoly asserted" *General Electric Company v. Wabash Appliance Corporation et* supra, at 468. Claims thus constructed provide no guidance as to medicaments employed, levels for providing therapeutic benefit, or provide notice for those practicing in the art, limits of protection. Simply stated, the presented claims are an invitation to experiment, not reciting a specific medicament regimen useful for practicing the instant invention.

Applicant's arguments filed August 31, 2004 averring the screening method for GHS being well-known have been considered, but are not found persuasive. As discussed above, there is no specific information with regard to the structural, physical, or chemical characteristics of the compounds recited is being provided in the instant specification. The claims read on all GHS, without providing the criteria of the suitable GHS compound. Therefore, one of skilled in the art would be required to perform undue experimentation to ascertain the GHS suitable for practicing the herein claimed method since any compounds known to man are potential candidates for practicing the herein claimed method.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-14 and 17-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Carpino'369 (WO97/24369 from the IDS filed December 3, 2001).

Carpino'369 teaches the elected compound as the preferred growth hormone secretagogues (See the abstract and claims 24-26, page 12, lines 20-25). Carpino'369 also teaches the compound can be administered in various dosage forms such as tablet and capsules, routes of administration such as oral, and different regimens such as in divided dosages (See page 31, line 10, also page 45, lines 9- page 46, line 18). Carpino'369 also teaches the effective dosage of the GHS compounds as 0.01-5mg/kg. Carpino'369 teaches the elected compound can be used to treat osteoporosis and strengthen bones (See particularly the abstract, page 29, lines 18-21).

Carpino'369 does not expressly teach the GHS compound to be administered intermittently, twice daily, three times daily, every two, three, four, or five days, three times, or four times weekly. Carpino'369 does not expressly teach the GHS compound to be administered as controlled and/or immediate release. Carpino'369 does not expressly teach the dosage of the GHS compound as 1-10mg daily.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to administer the elected GHS compound in the herein claimed dosage and regimen.

One of ordinary skill in the art would have been motivated to administer the elected GHS compound in the herein claimed dosage and regimen. As anyone of ordinary skill in the art will appreciate, preferred dosages are merely exemplary and serve as useful guideposts for the physician. There are, however, many reasons for varying dosages, including by orders of magnitude; for instance, an extremely heavy patient or one having an unusually severe infection would require a correspondingly higher dosage. Furthermore, it is routine during animal and clinical studies to dramatically vary dosage to obtain data on parameters such as toxicity. Therefore, the optimization of result effect parameters (e.g., dosage range, dosing regimens) for achieving various therapeutic effects is obvious as being within the skill of the artisan.

Response to arguments

Applicant's arguments filed August 31, 2004 averring the cited prior art's failure to provide motivation to administer the elected GHS compound intermittently since most

pharmaceutical agents are administered daily have been considered, but are not found persuasive. It is within the purview of skilled artisan to optimize the effect of the drug based on the physiochemical properties of the drugs. For example, some bisphosphonates are having a very long half-life that those compounds may be administered couple times a year! It is not unusual to one of ordinary skill in the art to adjust and optimize dosing regimen in view of the patients condition, concomitant medical treatment, renal and/or hepatic functions, dosage, toxicity of the drugs, and half-life of the drug.

Applicant's arguments filed August 31, 2004 averring the unexpected high plasma concentration of the elected GHS compound by intermitantly administration have been considered, but are not found persuasive. Examiner notes that it is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). It is not clear as to the effect of intermittent administration has on the level of growth hormone is being represented in page 63. The only group that produce a growth hormone level of 5ng/ml or above after 4 weeks is the one the receiving 6mg IR + 10mg CR. It is not clear as to what is the level of growth

hormone after 4 weeks for the group that receive GHS compound daily. And even if the instant specification demonstrates unexpected results, the results disclosed in the instant specification are not commensurate with the scope recited herein. Therefore, the claims are still properly rejected under 35 USC 103(a).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax

phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Primary Examiner
Art Unit 1617